

Claims:

1. A method for identifying a compound which reduces the activity of thymidylate synthase comprising the steps of:
  - 5 growing in the absence of a test compound a first culture of mammalian cells comprising a DNA construct comprising functionally joined together in the 5' to 3' direction of transcription, (i) a promoter, (ii) a TBE cassette comprising at least one copy of TBE 1 in the forward orientation (SEQ ID NO: 2) or reverse orientation (SEQ ID NO: 4) and at least one copy of TBE2 in the forward  
10 orientation (SEQ ID NO:3) or reverse orientation (SEQ ID NO:5); and (iii) a reporter gene; wherein the TBE cassette and the reporter gene are operably linked to the promoter.  
growing a second culture of the cells in the presence of the test compound;
  - 15 lysing the first culture and the second culture to produce a first lysate and a second lysate respectively;  
assaying the first lysate and the second lysate for activity of the protein encoded by the reporter gene; and  
20 comparing the activities of the first lysate and the second lysate, wherein an increase in the activity in the second lysate is indicative of a compound which reduces the activity of thymidylate synthase.
2. The method of claim 1, wherein the at least one copy of TBE1 and the at least one copy of TBE2 are separated by a DNA spacer of about 20 nucleotides.  
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3. The method of claim 1, wherein the reporter gene is luciferase gene.
4. The method of claim 1, wherein the promoter is the ERG-1 promoter.
- 30 5. The method of claim 1, wherein the TBE cassette has the sequence of SEQ ID NO:1.

6. The method of claim 1, wherein the DNA construct is contained in a vector.
7. The method of claim 6, wherein the vector containing the DNA construct is plasmid pG3E1-2TBE.
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8. A method for identifying a compound which reduces the activity of thymidylate synthase comprising the steps of:
- growing in the absence of a test compound a first culture of mammalian cells comprising a DNA construct comprising functionally joined together in the
- 10 5' to 3' direction of transcription (i) a promoter; (ii) a TBE cassette comprising at least one copy of TBE1 in the forward orientation (SEQ ID NO:2) or reverse orientation (SEQ ID NO:4) and at least one copy of TBE2 in the forward orientation (SEQ ID NO:3) or reverse orientation (SEQ ID NO:5); and (iii) a reporter gene, the TBE cassette and the reporter gene being operably linked to the
- 15 promoter, wherein the DNA construct is stably maintained in the cells;
- growing a second culture of the cells in the presence of the test compound;
- lysing the first culture and the second culture to produce a first lysate and a second lysate respectively;
- 20 assaying the first lysate and second lysate for activity of the protein encoded by the reporter gene; and
- comparing the activities of the first lysate and the second lysate, wherein an increase in the activity in the second lysate is indicative of a compound which reduces the activity of thymidylate synthase.
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9. The method of claim 8, wherein the at least copy of TBE1 and the at least one copy of TBE2 are separated by a DNA spacer of about 20 nucleotides.
10. The method of claim 8, wherein the reporter gene is luciferase gene.
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11. The method of claim 8, wherein the promoter is the ERG-1 promoter.

12. The method of claim 8, wherein the TBE cassette has the sequence of SEQ ID NO:1.
13. The method of claim 8, wherein the DNA construct is contained in a vector.
- 5 14. The method of claim 13, wherein the vector containing the DNA construct is plasmid pGE31-2TBE1-Neo.
- 10 15. A DNA construct comprising:  
functionally joined together in the 5' to 3' direction of transcription, (i) a promoter, (ii) a TBE cassette comprising at least one copy of TBE 1 in the forward orientation (SEQ ID NO: 2) or reverse orientation (SEQ ID NO: 4) and at least one copy of TBE2 in the forward orientation (SEQ ID NO:3) or reverse orientation (SEQ ID NO:5); and (iii) a reporter gene; wherein the TBE cassette and the reporter gene are operably linked to the promoter.
- 15 16. The method of claim 15, wherein the at least copy of TBE1 and the at least one copy of TBE2 are separated by a DNA spacer of about 20 nucleotides.
- 20 17. The construct of claim 15, wherein the reporter gene is luciferase gene.
18. The construct of claim 15, wherein the promoter is the ERG-1 promoter.
- 25 19. The construct of claim 15, wherein the TBE cassette has the sequence of SEQ ID NO:1.
20. The construct of claim 15, wherein the DNA construct is contained in a vector.
- 30 21. The construct of claim 20, wherein the vector containing the DNA construct is plasmid pGE1-2TBE.
22. The construct of claim 15 further comprising a selectable marker.

23. The construct of claim 22, wherein the selectable marker is neomycin resistance gene.
- 5 24. The construct of claim 23, wherein the DNA construct is contained in the plasmid pG3E1-2TBE-Neo.
25. Mammalian cells stably transfected with a vector comprising a DNA construct comprising:
- 10 functionally joined together in the 5' to 3' direction of transcription, (i) a promoter, (ii) a TBE cassette comprising at least one copy of TBE 1 in the forward orientation (SEQ ID NO: 2) or reverse orientation (SEQ ID NO: 4) and at least one copy of TBE2 in the forward orientation (SEQ ID NO:3) or reverse orientation (SEQ ID NO:5); and (iii) a reporter gene; wherein the TBE cassette and the reporter gene are operably linked to the promoter; and
- 15 a selectable marker gene.
26. The cells of claim 25, wherein the cells are human cells.
- 20 27. The cell of claim 26, wherein the cells are H630 colon tumor cells or RKO colon tumor cells.
28. The cells of claim 24, wherein the vector is the plasmid pG3E1-2TBE-Neo.